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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/077,171	02/15/2002	Pamela Sklar	2825.2026-001	3181
28120	7590	06/24/2004	EXAMINER	
ROPER & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			SITTON, JEHANNE SOUAYA	
			ART UNIT	PAPER NUMBER

1634

DATE MAILED: 06/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/077,171

Applicant(s)

SKLAR ET AL.

Examiner

Jehanne Souaya Sitton

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 13 April 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 11-21, 24 and 25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11-21, 24, and 25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

1. Currently, claims 11-21 and 24-25 are pending in the instant application. The amendment and the arguments have been thoroughly reviewed but are insufficient to place the instant application in condition for allowance. The following rejections are either reiterated or newly applied as necessitated by amendment. This action is FINAL.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***New Grounds of Objection and Rejection***

##### ***Claim Objections***

3. Claims 14 and 20 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 11 and 16 are drawn to methods which comprise a step of determining the identity of nucleotide position 31 as numbered in SEQ ID NO: 1. One of skill in the art, reading this claim, would determine that such was drawn to determining the identity of the nucleotide at position 31, not another nucleotide at a different position. However, claims 14 and 20, which are dependent from claims 11 and 16 respectively, recite ascertaining the nucleotide at position 858 using SEQ ID NO: 3. As such, the claims do not further limit claims 11 and 16. Appropriate correction is required.

##### ***Response to Arguments***

4. The response asserts that the linkage disequilibrium between position 31 and position 858 enables a skilled artisan to determine the nucleotide at position 31. This

Art Unit: 1634

argument has been thoroughly reviewed but was not found persuasive because the issue at hand is not with regard to 35 USC 112/first paragraph. Claim 11 is only drawn to determining the nucleotide at position 31, it does not recite "or nucleotides in linkage disequilibrium". Accordingly, the recitation of claims 14 and 20 do not further limit claims 11 and 16 respectively.

***Claim Rejections - 35 USC § 101***

5. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 11-12, and 16-18 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 11 and 16 have been amended to remove the positive active step of "obtaining a DNA sample from an individual to be assessed". As such, the recitation of 'determining' is the only step present in the claim which encompasses a mental step.

***Claim Rejections - 35 USC § 112***

7. Claims 11-21 and 24-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of predicting the likelihood that an individual will be diagnosed with bipolar disorder comprising detecting the nucleotide present at nucleotide position 31 of brain derived neurotrophic factor gene, as numbered in SEQ ID NO: 1, in a DNA sample from an individual to be assessed, wherein the presence of a "A" at position 31 indicates that the individual has an increased

Art Unit: 1634

likelihood of being diagnosed with a bipolar disorder as compared with an individual having at “T” at that position and wherein the presence of a “T” at position 31 indicates that the individual has a reduced likelihood of being diagnosed with a bipolar disorder as compared to an individual having an “A” at that position, does not reasonably provide enablement for methods wherein the actual nucleotide specifically at position 31 is not determined, but where nucleotides in linkage disequilibrium are determined. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claims 14 and 20 are drawn to determining the nucleotide at position 31 by “ascertaining the nucleotide at position 858”. It is noted that this dependency renders the use of the term “at position 31” in claims 11 and 16, not only indefinite and unclear, but also broader than would generally be accepted by one of skill in the art. Although the specification teaches, at page 25, that the T allele at position 31 was found to be “in nearly complete linkage disequilibrium” with the A allele at position 858, the identity of the allele at position 858 does not necessarily indicate the actual identity of the allele at position 31. For example, no data is presented as to what the presence of a T or a C at position 858 would indicate in terms of the identity of the allele at position 31. Further, claims 13, 15, 19, and 21 are not limited to position 858. In such claims, it is unclear as to what the scope of the term “corresponding” is. For example, such could encompass other alleles that are in linkage disequilibrium with position 31 or 858 of SEQ ID NO: 1. However, such is also not necessarily predictive of the allele of position 31. Sklar et al (Molecular Psychiatry; 2002, vol. 7, pp 579-593) teach of a number of different

Art Unit: 1634

haplotypes that are found for BDNF (see table 4). For example, in the Hopkins dataset, 13 different haplotypes were found (page 588, 2<sup>nd</sup> col. Last para). While the SNPS in table 3 were found to be in “strong linkage disequilibrium” (see page 588, col. 2, first sentence of first full para) the presence of so many haplotypes shows that linkage disequilibrium will not always determine the identity of the allele of a certain position based on the identity of an allele at a position in linkage disequilibrium with it. Table 3 shows that patients with a G at position a39, had either an A or a T at position a40 (a40 is the same SNP as position 31 of instant SEQ ID NO: 1). Thus, while the specification provides an association between a decreased likelihood of bipolar disorder and a T at position 31 as compared to an A at that position, the specification has not established a predictable correlation that the identity of the allele at position 31 can be determined by determining the identity of an allele “corresponding to position 31 of SEQ ID NO: 1”. As neither the specification nor the claim define the metes and bounds of such recitation, the scope of the term “corresponding” is very large, and minimally encompasses alleles in linkage disequilibrium. However, as evidenced by the teachings in the prior art, determining the identity of an allele (ie: allele 1) does not necessarily indicate the true identity of a nucleotide of an allele in linkage disequilibrium with allele 1. Trial and error analysis would be required for the skilled artisan to determine the identity of the nucleotide at position 31 of SEQ ID NO: 1 by determining the identity of an allele “corresponding” to position 31 of SEQ ID NO: 1. The outcome of such analysis is unpredictable, as evidence by the art, and is therefor considered undue.

***Response to Arguments***

8. The response traverses that the term “corresponding” in claims 13 and 19 have been canceled. This argument was thoroughly reviewed but was unpersuasive because claims 14 and 20 continue to recite ‘nucleotide at position 31 is determined by ascertaining the nucleotide at position 858...’. As evidenced by the teaching of Sklar, determining the identity of an allele (ie: allele 1) does not necessarily indicate the true identity of a nucleotide of an allele in linkage disequilibrium with allele 1. Looking at table 4 of Sklar, it is clear that detecting a G at a39, could indicate either a T or an A at a40. As such, the rejection is maintained.

9. Claims 11-21 and 24-25 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 11 and 16 have been amended to remove the positive active step of “obtaining a DNA sample from an individual to be assessed”. As such, the recitation of ‘determining’ is the only step present in the claim which encompasses a mental step. As such, the claims do not contain any positive active steps.

***Maintained Rejections***

***Claim Rejections - 35 USC § 112***

10. Claims 11-21 and newly added claims 24-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Art Unit: 1634

With regard to claims 11 and 16, where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The recitation of “at nucleotide position 31” in claims 11 and 16 appears to be used by the claim to mean “not necessarily *at* position 31”. The meaning of this recitation is unclear based on the improper dependency of claims 14 and 20 respectively. If the claims are not improperly dependent, than the use of “determining the nucleotide present at nucleotide position 31” is not consistent with the accepted meaning because one of skill in the art would take that to mean actually testing the identity of a nucleotide *at* position 31, not another position, as the claims appear to intend. The term is indefinite because the specification does not clearly redefine the term.

### ***Response to Arguments***

11. The response does not address this rejection.

### ***Conclusion***

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).



Art Unit: 1634

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. No claims are allowable.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

Note: The examiner's name has changed from Jehanne Souaya to Jehanne Sitton. All future correspondence to the examiner should reflect the change in name.

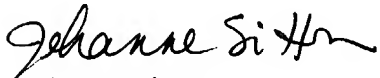
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571) 272-0782. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Art Unit: 1634

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Jehanne Sitton

Primary Examiner

Art Unit 1634

6/22/04